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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,092	07/10/2000	Edwin W. Ades	68430	9419

23859 7590 12/11/2003

NEEDLE & ROSENBERG, P.C.
SUITE 1000
999 PEACHTREE STREET
ATLANTA, GA 30309-3915

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	19

DATE MAILED: 12/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/613,092	Applicant(s) ADES ET AL.	
	Examiner S. Devi, Ph.D.	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *2-10 and 12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) *11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

SEQ ID NO: 6

```
RESULT 6
AAR14929
ID   AAR14929 standard; Protein; 12 AA.
XX
AC   AAR14929;
XX
DT   13-FEB-1992  (first entry)
XX
DE   OT-2 antibody binding peptide (2).
XX
KW   Monoclonal antibody; antigen; immunogen; Factor XII; epitope.
XX
OS   Synthetic.
XX
PN   WO9117258-A.
XX
PD   14-NOV-1991.
XX
PF   01-MAY-1991;   91WO-US02990.
XX
PR   10-MAY-1990;   90US-0521820.
XX
PA   (CETU ) CETUS CORP.
XX
PI   Nuijens JH,  Huijbregts CCM,  Hack CE;
XX
DR   WPI; 1991-353779/48.
XX
PT   Treatment of sepsis using inhibitor of factor XII activation -
PT   comprises use of new OT-2 antibody
XX
PS   Claim 15,17; Page 24; 32pp; English.
XX
CC   Based on the known amino acid sequence of Factor XII, peptides
CC   corresp. to neutralising epitopes of the mol. are synthesised and
CC   used as immunogens to produce antibody.  The pref. peptides are
CC   represented in AAR14928-30.  Amino acid Asp in this sequence =
CC   residue 442.
XX
SQ   Sequence   12 AA;

  Query Match          40.0%;  Score 6;  DB 12;  Length 12;
  Best Local Similarity  100.0%;  Pred. No. 4.1;
  Matches    6;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       2 SYQHDL 7
           ||||||
Db       5 SYQHDL 10
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RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 09/30/03 (paper no. 18) in response to the non-final office Action mailed 04/30/03 (paper no. 17). With this, Applicants have amended the specification by adding a paragraph at the beginning of the specification. Applicants state that the instant specification is a Continuation-in-part of the PCT application PCT/US99/04326, filed 02/26/99, which claims domestic priority to the provisional application, SN 60/076,565, filed 03/02/1998.

Status of Claims

2) No claims have been amended via the amendment filed 09/30/03.

Claims 1-20 are pending.

Claims 1 and 11 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Maintained

5) The objection to the specification made in paragraph 8(b) of the Office Action mailed 09/17/02 (paper no. 13) and maintained in paragraph 7 of the Office Action mailed 04/30/03 (paper no. 17) with regard to sequence non-compliance is maintained for reasons set forth therein.
It is noted that neither a Sequence Listing is submitted along with the amendments filed 02/24/03 and 09/30/03, nor has the specification on page 28, line 27 and page 29 line 9 been amended identifying sequences 'CYGG' and "LXCC' with a SEQ ID number. The objection stands.

It is noted that Applicants have not addressed or responded to this objection in their response filed 09/30/03.

Specification - New Matter

6) The first paragraph to the specification added via the amendment filed 09/30/03 (paper no.18) is objected to under 35 U.S.C. § 132, because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The recitation 'incorporation by reference' is new matter. For the incorporation by reference to be effective as a proper safeguard against the omission of a portion of a prior application, the incorporation by reference statement must be included in the specification-as-filed, or transmittal letter-as-filed, or in an amendment specifically referred to an oath or declaration executing the application. An incorporation by reference statement added after an application's filing date is not effective because no new matter can be added to an application after its filing date. See 35 U.S.C § 132(a). If an incorporation by reference statement is included in an amendment to the specification to add a benefit claim under 35 U.S.C. 120 after the filing date of the application, the amendment would not be proper. When a benefit claim under 35 U.S.C. 120 is submitted after the filing of an application, the reference to the prior application cannot include an incorporation by reference statement of the prior application. See *Dart Indus. v. Banner*, 636 F.2d 684, 207 USPQ 273 (C.A.D.C 1980).

Rejection(s) Withdrawn

7) The rejection of claim 1 made in paragraph 15 of the Office Action mailed 04/30/03 (paper no. 17) as being unpatentable over Ades *et al.* (WO 99/45121 - Applicants' IDS) ('121) in view of in view of Tam (*In*: *Peptide Antigens*: *A Practical Approach*. (Ed) Wisdom G.B. IRL Press, Oxford University Press, New York, 1993, pp. 83-90), or Huang *et al.* (*Mol. Immunol.* 31: 1191-1199, 1994), is withdrawn in light of Applicants' claim of priority to PCT/US99/04326 and the US provisional application 60/076,565.

Rejection(s) under 35 U.S.C. § 103

8) Claim 1 is rejected under 35 U.S.C § 103(a) as being unpatentable over Sampson *et al.* (US 6,217,884) in view of Tam (*In*: *Peptide Antigens*: *A Practical Approach*. (Ed) Wisdom G.B. IRL Press, Oxford University Press, New York, pp. 83-90. 1994 - already of record), or Huang *et al.* (*Mol. Immunol.* 31: 1191-1199, 1994 - already of record) and Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988).

The reference of Sampson *et al.* is applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C § 102 and accordingly is not disqualified under U.S.C 103(a).

It is noted that claim 1 neither places a limit on the size or length of the peptide claimed, nor does it structurally identify the peptide by a SEQ ID number.

Sampson *et al.* disclosed a fragment (i.e., peptide) of a 37 kDa protein of *S. pneumoniae* which is used as a vaccine component as well as a reagent for identifying host antibodies raised against *S. pneumoniae* during infection. The specific monoclonal antibodies used are 1E7A3D7C2; 1B6E12H9; 3C4D5C7; 4E9G9C3; 4H5C10F3; and 6F6F9C8; and 8G12G11B10 (see abstract; and column 7, lines 40-46; all of columns 11 and 12 including the paragraph bridging columns 11 and 12; and column 13, lines 1-46). The composition comprises a unique fragment (i.e., a peptide) of the 37-kDa pneumococcal surface adhesion protein (i.e., PsaA) for use in inoculating a host such that the polypeptide fragment generates an active immune response in the host which protects the host from infection (see column 13, seventh full paragraph). The composition comprises a pharmaceutically acceptable carrier and adjuvants (see column 14, lines 1-24). Synthetic peptides disclosed include shorter and larger peptides (see last paragraph in column 10) or partial polypeptides (see first full paragraph). The immunoreactive fragment of the 37 kDa pneumococcal surface adhesin protein is at least about 6 consecutive amino acids (i.e., inclusive of 10-15, 12-22 or 15 amino acid residues in length) having the ability to evoke an immune response (see lines 52-59 in column 11). The fragments are produced by selected modifications provided the immunogenicity of the peptide is not significantly impaired compared to the 37 kDa pneumococcal surface adhesin protein (see paragraph bridging columns 11).

However, it was routine and conventional in the art at the time of the invention to modify a peptide as a multiple antigen peptide with a built-in-adjuvant for the purpose of providing a very high density of the peptide epitope. For instance, see the teachings of Tam on pages 87, 83 and 84.

Huang *et al.* taught the disadvantage of presenting a peptide as a peptide-protein carrier or as an adjuvant mixture, the disadvantage being the difficulty in defining the chemical composition and stoichiometry of such a mixture. Huang *et al.* taught the advantages of presenting a peptide via a MAP system. Huang *et al.* taught that the MAP system permits the amplification of antigens 4 to 8-

fold to attain a macromolecule and avoids the use of a protein carrier as well as attendant structural ambiguity. See page 1191.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify Sampson' PsaA fragment or peptide as a multiple antigen peptide with a built-in-adjuvant as taught by Tam, to produce the instant invention, with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of presenting Nuijens' PsaA peptide as a multiple antigen peptide with a built-in-adjuvant for the purpose of advantageously providing a very high density of the peptide mimic as taught by Tam, or for avoiding the use of a protein carrier and avoiding structural ambiguity of a conjugate as taught by Huang *et al.*

Claim 1 is *prima facie* obvious over the prior art of record.

9) Claim 1 is rejected under 35 U.S.C § 103(a) as being unpatentable over Nuijens *et al.* (WO 9117258) in view of Tam (*In*: *Peptide Antigens*: *A Practical Approach*. (Ed) Wisdom G.B. IRL Press, Oxford University Press, New York, pp. 83-90. 1994 - already of record), or Huang *et al.* (*Mol. Immunol.* 31: 1191-1199, 1994 - already of record) and Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988).

It is noted that claim 1 neither places a size or length limit of the recited peptide, nor identifies the peptide by a SEQ ID number.

Nuijens *et al.* disclosed a therapeutic or prophylactic composition comprising a peptide having the sequence, SYQHDL, which shows 100% sequence identity with a fragment of the instantly claimed peptide of SEQ ID NO: 10. See the attached sequence alignment; and Example II of Nuijens *et al.* The peptide is conjugated to a suitable carrier to enhance elicitation of an antibody response. Although Nuijens *et al.* are silent about the binding of the peptide to a monoclonal antibody obtained in response to immunizing an animal with *S. pneumoniae* PsaA as recited in claim 1, the prior art peptide sequence is viewed as the same as the Applicants' claimed peptide. The Office's position that Nuijens' peptide is the same as the Applicants' peptide is based upon the fact that every characteristic overlapping in Nuijens' and Applicants' disclosure are the same. In spite of the fact that Nuijens *et al.* are silent about the binding of the peptide to a monoclonal antibody obtained in response to immunizing an animal with *S. pneumoniae* PsaA, since the prior art peptide is

structurally the same as the instantly claimed peptide, the peptide is expected to bind immunospecifically to the Applicants' monoclonal antibody which was inaccessible to Nuijens *et al.* at that time. The property of binding to the specific monoclonal antibody recited by the Applicants is viewed as an uncharacterized functional feature intrinsic to the peptide of Nuijens *et al.* Due to the region of 100% sequence identity, the peptide of the prior art is expected to bind immunospecifically to a monoclonal antibody as recited, because the art recognizes that the smallest peptides which elicit antibodies that bind to the original full length protein are 6 amino acids in length. See the first sentence under 'Size of the Peptide' on page 76 of Harlow *et al.*

Nuijens *et al.* differ from the instant invention in not expressly disclosing that the PsaA peptide is present as a multiple antigenic peptide.

However, it was routine and conventional in the art at the time of the invention to modify a peptide as a multiple antigen peptide with a built-in-adjuvant for the purpose of providing a very high density of the peptide epitope. For instance, see the teachings of Tam on pages 87, 83 and 84.

Huang *et al.* taught the disadvantage of presenting a peptide as a peptide-protein carrier or as an adjuvant mixture, the disadvantage being the difficulty in defining the chemical composition and stoichiometry of such a mixture. Huang *et al.* taught the advantages of presenting a peptide via a MAP system. Huang *et al.* taught that the MAP system permits the amplification of antigens 4 to 8-fold to attain a macromolecule and avoids the use of a protein carrier as well as attendant structural ambiguity. See page 1191.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify Nuijens' PsaA peptide as a multiple antigen peptide with a built-in-adjuvant as taught by Tam, to produce the instant invention, with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of presenting Nuijens' PsaA peptide as a multiple antigen peptide with a built-in-adjuvant for the purpose of advantageously providing a very high density of the peptide mimic as taught by Tam, or for avoiding the use of a protein carrier and avoiding structural ambiguity of a conjugate as taught by Huang *et al.*

Claim 1 is *prima facie* obvious over the prior art of record.

Remarks

10) Claim 1 stands rejected. Claim 11 stands objected to for being dependent from a rejected claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claim.

11) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center receives transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

12) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December, 2003

SD.
S. DEVI, PH.D.
PRIMARY EXAMINER